

ABSTRACT

Methods of using NMR spectroscopy for identifying ligands that bind to structurally uncharacterized proteins, and for improving the binding affinity of ligands for biological targets, which in one aspect comprises:

- a) preparing first NMR spectra of a first complex comprising the biological target and a paramagnetically labeled derivative of a first ligand;
- b) preparing second NMR spectra of a second complex comprising the biological target and a second ligand; and
- c) analyzing the spectra to determine whether the second ligand binds to the biological target within the paramagnetic zone of the paramagnetically labeled derivative;

wherein steps (a) and (b) are performed simultaneously, consecutively, or in any order.